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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,365	09/21/2005	Jean-Charles Quirion	QUIRION1	1397
1444 7590 12/23/2008 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303				
EXAMINER KRISHNAN, GANAPATHY				
ART UNIT		PAPER NUMBER		
1623				
MAIL DATE		DELIVERY MODE		
12/23/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/522,365

Applicant(s)

QUIRION ET AL.

Examiner

Ganapathy Krishnan

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SG/US)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

The amendment filed 9/18/2008 has been received, entered and carefully considered.

The following information provided in the amendment affects the instant application:

1. Claims 7-19 have been canceled.
 2. Claim 6 has been amended.
 3. Remarks drawn to rejections under 35 USC 103(a)
- Claims 1-6 are pending in the case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marcotte et al (Tetrahedron Letters, 2001, 42, 5879-5882; document # AE cited in IDS of 1/25/2005) in view of Wong et al (Bioorganic & Medicinal Chemistry Letters, 1998, 8, 2333-2338) and,

The rejection of Claims 4-6 under 35 U.S.C. 103(a) as being unpatentable over Lerner et al (J. Org. Chem. 1979, 44(19), 3368-3373) in combination with Furstner (Synthesis, 1989, 571-590) is being maintained for reasons of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Regarding the rejections under 35 USC 103 applicants have traversed the rejection arguing that:

1. Neither Marcotte nor Wong teach or suggest that in addition to a lateral chain bearing a CF₂ and an additional hydroxyl or protected oxygen will be important for biological activity.
2. Applicants' compound has a hydroxyl at the anomeric position, which allows the sugar to exist in different forms in solution and also have possible interaction with receptors such as through hydrogen bonding. It is not obvious that having a hydroxyl and a CF₂ at the anomeric position may lead to stable compounds that have biological utility.

3. Regarding the rejection of claims 4-6, applicants argue that the 6-membered lactone and the reagent $\text{BrCF}_2\text{CO}_2\text{Et}$ are different except zinc. It is not evident that applicants' process would work. There is no indication that the Reformatsky reaction would work on a lactone since one of skill in the art would assume that it is not a good electrophile. Enolization and the addition of a second ester moiety can occur. The zinc derivative (page 7 of applicants' remarks) prevents the addition of a second ester moiety. This means that even the slightest traces of proton source has to be avoided.

4. Applicants results on inhibition tests show that their compounds containing a hydroxyl and a CF_2 group at the anomeric carbon show improvement in terms of biological activity compared to the compounds of Wong and Marcotte.

Applicants' arguments have been considered but are not found to be persuasive.

Marcotte et al teach a C-glycoside (Structure 1, page 5879) that has a CF_2 group and an alkyl chain that is functionalized with an amine group and an acid function. Marcotte teaches that structure 1 is a glycoserine or glycothreonine (page 5879, right column, lines 8-9). According to Marcotte replacement of the anomeric oxygen with a gem difluoromethylene group induces differences in the biological functions of compounds of structure 1, which are also hydrolytically stable. Hence, preparation of new derivatives comprising a gemdifluoromethylene group in the place of anomeric oxygen is a promising avenue for the preparation of new glycoconjugate derivatives (page 5879, left column, lines 7-14). According to Wong these structures are useful as mimics of sialyl lewis X as inhibitors of E- and P-selectin (page 2333, abstract and first paragraph). Both Wong and Marcotte may not explicitly teach or suggest the presence of a hydroxyl and a CF_2 moiety at the anomeric carbon may produce compounds with biological

activity and stability. Marcotte teaches sugars with a CF_2 group at the anomeric position. One of skill in the art knows that sugars have a hydroxyl at the anomeric carbon. Wong's objective is to study the effect of structural modification on bonding affinity (page 2333, paragraph below structure). One of skill in the art also knows that bonding in sugars can occur through the hydroxyl group and would have the hydroxyl at the anomeric carbon too. This and the teaching of Marcotte regarding the use of the difluoromethylene group suggests to one of skill in the art to make sugars having a combination of both these structural features in order to look for derivatives with enhanced biological activity. One of skill in the art would look for enhanced binding as indicated by test results provided by the applicants.

Regarding the method of making the compounds as instantly claimed, it may have been evident to one of skill in the art that a lactone may not be a suitable electrophile for reaction with $\text{BrCF}_2\text{CO}_2\text{Et}$ and its reaction with the carbonyl group of the lactone may not be as facile as with $\text{BrCH}_2\text{CO}_2\text{Et}$. One of skill in the art would expect the zinc derivative (shown at page 7 of applicants' remarks) to form in the Reformatsky reaction and also knows that such an intermediate proton source should be kept out of the reaction medium for the reaction to proceed. Knowing this fact one of skill in the art would not perform the reaction of $\text{BrCF}_2\text{CO}_2\text{Et}$ with the lactone under the same conditions as the classical Reformatsky reaction of $\text{BrCH}_2\text{CO}_2\text{Et}$ with the lactone. One would alter conditions to induce the reaction. It is well within the skill level of the artisan to perform the reaction by altering the reaction conditions like temperature, reaction time, and also manipulate the order of addition of the reagents, performing the reaction under anhydrous conditions, etc., in order to make the reaction work. These are techniques well known to the artisan to be applied to any reaction for the purpose of optimization of reaction conditions.

Also, as taught by Furstner (page 575, right column, last paragraph through page 576, left column) the Reformatsky reaction of α -dihalo esters are influenced by reaction conditions. This teaching of Furstner would prompt one of skill in the art to optimize conditions for the reactivity of $\text{BrCF}_2\text{CO}_2\text{Et}$ with the lactone.

Conclusion

Claims 1-6 are rejected

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623